

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Please amend claims 1, 3-6, 8, 10-14, 16-20, and 22 as follows.

Please delete claims 2, 7, 9, 15, 21, 23, 36, and 37 as follows.

Claim 1. (amended) A label-free method for the classification of ~~cellular events~~,

~~wherein the classification is achieved through measuring~~ signal transduction from
stimulus-receptor interactions by the measurement of changes in the electrical properties
of cells incorporated into an electrical circuit after application of a stimulus,
the method comprising:

- (a) measuring a value of an electrical property after application of ~~for~~ at least one frequency
of the electromagnetic spectrum within a range of frequencies for ~~each~~ selected time
points during a selected period of time for the electric circuit comprising a cells with a
receptor having a known receptor type and a known messenger pathway;
- (b) selecting a reference time point corresponding to a time period immediately prior to
addition of a known receptor stimulus;
- (c) adding a the known stimulus to the electric circuit such that the stimulus is able to
interact with the receptor;
- (d) calculating changes in the value of the electrical property for each frequency by
subtracting the value of the measured electrical property for the reference time point
from the value of the measured electrical property for each time point subsequent to the
reference time point;

- (e) parameterizing the changes in the value of the electrical property for each time point, receptor, and stimulus;
- (f) and, ~~comparing the parameterized changes in the value of the electrical property to parameter sets of known messenger pathways to~~ assigning the parameterized changes in value of the electrical property to a known stimulus/receptor interaction class.

Claim 2. **(deleted)** ~~The method of claim 1 wherein the cellular events are chosen from the group comprising signal transduction from ligand/receptor interactions, cytotoxicity, apoptosis, tumor cell progression, and stem cell differentiation.~~

Claim 3. (amended) The method of claim 1, wherein the electrical properties ~~are chosen from the group comprising~~ comprise impedance phase, impedance magnitude, complex reflection coefficients, total circuit resistance, and total circuit capacitance.

Claim 4 (amended). The method of claim 1, wherein the at least one frequency within a range of frequencies includes frequencies in the electromagnetic spectrum and acoustic frequencies.

Claim 5 (amended). The method of claim 1, wherein the range of frequencies is 40Hz to 110MHz.

Claim 6 (amended). The method of claim 1, wherein the stimulus is a substance.

Claim 7 (deleted). ~~The method of claim 6, wherein the substance is a small molecule ligand.~~

Claim 8 (amended) . The method of claim 6, wherein the substance is a ligand, a protein, an antibody, a lipid, a carbohydrate, a nucleic acid, water, or an ion.

Claim 9 (deleted). The method of claim 1, wherein the classification is achieved in real time.

Claim 10 (amended). The method of claim 1, further comprising the steps of

- g) measuring the value of the electrical property for the electric circuit comprising cells for at least one frequency in a range of frequencies for ~~each~~ selected time points during a selected period of time for a cell with a known receptor type;
- h) selecting a reference time point corresponding to a time period immediately prior to addition of an unknown stimulus;
- i) adding the unknown stimulus to the circuit such that the stimulus is able to interact with the receptor;
- j) calculating changes in the value of the electrical property for each frequency by subtracting the value of the electrical property for the reference time point from the value of the electrical property for each ~~subsequent~~ time point subsequent to ~~after~~ addition of the unknown stimulus;
- k) parameterizing the changes in the value of the electrical property for each time point, receptor, and stimulus;

- l) comparing the parameterized changes in the value of the electrical property after addition of the unknown stimulus to the parameterized changes in value for known stimuli ~~changes in the value of the electrical properties for known stimuli~~ to correlate the changes in the value of the electrical property to a cellular response;
- m) and, assigning the cellular response to the unknown stimulus to a known substance/receptor interaction class and classifying the stimulus.

Claim 11 (amended). The method of claim 1, further comprising the steps of

- g) measuring the value of the electrical property for the electrical circuit comprising cells for at least one frequency within a range of frequencies for ~~each~~ selected time points during a selected period of time for a cell with an unknown receptor type;
- h) selecting a reference time point corresponding to a time period immediately prior to addition of a stimulus with a known response;
- i) adding the stimulus to the circuit such that the stimulus is able to interact with the receptor;
- j) calculating changes in the value of the electrical property for each frequency by subtracting the value of the electrical property for the reference time point from the value of the electrical property for each ~~subsequent~~ time point subsequent to ~~after~~ addition of the stimulus;

- k) parameterizing the changes in the value of the electrical property for each time point, receptor, and stimulus;
- l) comparing the parameterized changes in the value of the electrical property after addition of the stimulus to the parameterized changes in the value of the electrical properties for known receptors to correlate the changes in the value of the electrical property to a cellular response;
- m) and, assigning the cellular response of the unknown receptor to a known substance/receptor interaction class and classifying the receptor.

Claim 12 (amended). A label-free method for the classification of ~~cellular events~~ signal transduction from stimulus/receptor interactions,

wherein the classification is achieved through measuring changes in the complex impedance of cells incorporated into an electrical circuit after application of a receptor stimulus

the method comprising:

- a) measuring the complex impedance over at least one frequency of the electromagnetic spectrum in a range of frequencies for ~~each~~ selected time points during a selected period of time for the electric circuit comprising cells with a known receptor type and a known messenger pathway;
- b) selecting a reference time point corresponding to a time period immediately prior to addition of a known receptor stimulus;
- c) adding a the known stimulus to the electric circuit such that the stimulus is able to interact with the cell receptors;

- d) calculating changes in complex impedance for each frequency by subtracting the complex impedance for the reference time point from the complex impedance for each time point subsequent to the reference time point;
- e) parameterizing the changes in complex impedance for each time point, receptor, and stimulus;
- f) and, ~~comparing the parameterized changes in impedance to parameter sets of known messenger pathways to~~ assigning the parameterized changes in complex impedance to a known stimulus/receptor interaction class.

Claim 13 (amended). The method of claim 12, further comprising the steps of

- g) measuring the complex impedance over at least one frequency within a range of frequencies for each time point during a selected period of time for the electrical circuit comprising a-cells with a known receptor type;
- h) selecting a reference time point corresponding to a time period immediately prior to addition of an unknown stimulus;
- i) adding the unknown stimulus to the electrical circuit such that the stimulus is able to interact with the cell receptors;
- j) calculating changes in the complex impedance for each frequency by subtracting the value of the impedance for the reference time point from the value of the impedance for each ~~subsequent~~ time point after subsequent to addition of the unknown stimulus;
- k) parameterizing the changes in complex impedance for each time point, receptor, and stimulus;

- l) comparing the parameterized changes in the complex impedance after addition of the unknown stimulus to the parameterized changes in the complex impedance for known stimuli to correlate the parameterized changes in the complex impedance to a cellular response;
- m) and, assigning the cellular response to a known substance/receptor interaction class and classifying the stimulus.

Claim 14 (amended). The method of claim 12, further comprising the steps of

- a) measuring ~~an~~ the complex impedance over at least one frequency within a range of frequencies for each time point during a selected period of time for a the electric circuit comprising cells with an unknown receptor type;
- b) selecting a reference time point corresponding to a time period immediately prior to addition of a stimulus with a known response;
- c) adding the stimulus to the electrical circuit such that the stimulus is able to interact with the cell receptors;
- d) calculating changes in complex impedance for each frequency by subtracting the complex impedance for the reference time point from the complex impedance for each ~~subsequent~~ time point subsequent to ~~after~~ addition of the stimulus;
- e) parameterizing the changes in complex impedance for each time point, receptor, and stimulus;

- f) comparing the parameterized changes in complex impedance after addition of the stimulus to the parameterized changes in complex impedance for known receptors to correlate the parameterized changes in complex impedance to a cellular response;
- g) and, assigning the cellular response to a known substance/receptor interaction class and classifying the receptor.

Claim 15 (deleted). ~~The method of claim 12 wherein the cellular events are chosen from the group comprising signal transduction from ligand/receptor interactions, cytotoxicity, apoptosis, tumor cell progression, and stem cell differentiation.~~

Claim 16 (amended). The method of claim 12, wherein the changes in complex impedance are measured as resistance or reactance.

Claim 17 (amended). The method of claim 12, wherein the changes in complex impedance are measured as admittance, conductance, or susceptance.

Claim 18 (amended). The method of claim 12, wherein the at least one frequency of the electromagnetic spectrum in a range of frequencies includes frequencies in the electromagnetic spectrum and acoustic frequencies.

19 (amended). The method of claim 12, wherein the range of frequencies is 40Hz to 110MHz.

Claim 20 (amended). The method of claim, wherein the stimulus is a substance.

Claim 21 (deleted). ~~The method of claim 20, wherein the substance is a small molecule ligand.~~

Claim 22 (amended). The method of claim 20, wherein the substance is a ligand, a protein, an antibody, a lipid, a carbohydrate, a nucleic acid, water, or an ion.

Claim 23 (deleted). ~~The method of claim 12, wherein the classification is achieved in real-time.~~

36 (deleted). ~~The method of claim 1 wherein the cells are incorporated into an electrical circuit.~~

37 (deleted). ~~The method of claim 12 wherein the cells are incorporated into an electrical circuit.~~

Remarks:

Claim Objections

The informalities discussed in the Claim Objections section of the Office Action mailed April 18, 2006 have been corrected.

In claim 1, line 3, a comma has been added after 'stimulus'.

In claim 2-23, a comma has been added after the recitation of the parent claim.

The preamble to claim 1 has been re-written as suggested by the Examiner.

Applicant respectfully asserts that the Claim Objections have been overcome and respectfully requests reconsideration.